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"Report on some of the Changes produced on Liver Cells by the Action of some Organic and Inorganic Compounds."

By T. LAUDER BRUNTON, M.D., F.R.S., and S. DELÉPINE, M.B. Received March 14, 1894.

We have, on a former occasion, given an account of the *scope of the investigation, and of the methods used, of some preliminary observations** which we have found it necessary to make.

Briefly speaking, our object was to ascertain the action of drugs on the cells of the liver and to connect, if possible, the changes in the cells with the physiological action of the drugs and their chemical structure.

Certain drugs were selected by one of us (Brunton) as being most suitable for this investigation. These drugs were the following :—

Benzene	$C_6H_5 \cdot H$
Phenol	$C_6H_5 \cdot OH$
Toluene	$C_6H_5 \cdot CH_3$
Aniline	$C_6H_5 \cdot NH_2$
Toluylene diamine (meta)	$C_6H_3 \begin{cases} CH_3\ (1) \\ NH_2\ (3) \\ NH_2\ (4) \end{cases}$
Chrysophanic acid	$C_{10}H_4O_4$
Pilocarpine nitrate	$C_{11}H_{16}N_2O_3 \cdot HNO_3$
Atropine	$(C_{17}H_{23}NO_3)_2H_2SO_4$
Ammonia	NH_3
Ammonium chloride	$NH_4 \cdot Cl$
Nitric acid	HNO_3
Sodium iodide	NaI

We have recorded the *various appearances which we have observed as the result of the purely physiological stimulation of the liver produced by the ingestion and digestion of a meal*, and have noticed that *the most important changes indicating various states of activity were :—*

1. The size of the cells.
2. The distinctness of the mitoma and of the cellular cleavage.

* 'Roy. Soc. Proc.,' Oct. 22, 1891, vol. 50, p. 209, and Paper placed in the Archives.

3. The size and arrangement of the meshes of the mitoma of the cells.

4. The size of the biliary canaliculi.

5. The amount and distribution of the glycogen in the cells and in the lobules of the organ.

6. The amount and distribution of granules giving the reaction characteristic of inorganic ferric salts.*

We also recorded changes affecting other parts, but we need not consider them for the present.

We will now give an *account of the appearances produced in the liver soon after the administration of the compounds mentioned above, either subcutaneously, by the rectum, or by the mouth* (the latter in only two cases) :—

1. To rabbits that had taken a moderate amount of food (50 grams of carrots from 7 to 9 hrs. before death—in two cases only the time was less than 7 hrs.) ;

2. To rabbits that had not been fed for at least 24 hrs. before death.

To estimate the changes produced, the organs of animals to which drugs had been administered were compared in each case with those of animals in the same stage of digestion, but to which no drug had been administered. Thus, when we say that a drug causes an enlargement of the meshes of the mitoma, or renders them more distinct or indistinct, or causes an accumulation of iron, we always mean that *the state in which the cells would have been at the same stage of digestion has been modified in the direction indicated.*

As the measurements of cells and parts of cells necessitate the careful drawing of a large number of cells with the camera lucida, the report, in its final shape, cannot yet be given, but, as all the appearances observed have been taken note of during the progress of the investigation, we are in position to give an idea of the results which have so far been obtained, but which we are not yet able to express in numbers, and compare as accurately as we hope to do when all our measurements are completed.

Action of Pilocarpine on a Fasting Liver.

A.—*Last food* given 25 hrs. before death.

Pilocarpine nitrate (grain $\frac{2}{3}$ = gram 0·042, dissolved in 10 c.c. of water) was injected into the rectum 1 hr. and 28 mins. before death.

* *Loc. cit.*, and also "Contribution to the Study of the Vertebrate Liver," 'Roy. Soc. Proc.,' Nov. 20, 1890, vol. 49, p. 64; "On the Normal Storage of Iron in the Liver," 'Practitioner,' vol. 45, p. 94.

B.—There were very few psorosperms in the liver, which was of small size.

Cells small, or of medium size.

Outlines of the cells and the mitoma much clearer than normal.

Meshes of the mitoma pretty large; some grouped round the lateral bile canaliculi.

Main and lateral bile canaliculi very distinct and very large.

Glycogen reaction normal, *i.e.*, doubtful and diffuse. Only slight traces of *sugar* could be obtained in 24 hrs. after death.

Iron reaction less marked than normal.

C.—The state of the mitoma of the cells, and the amount of iron indicate secretory activity.

This may be taken as a type of liver in a state of secretory activity.

Action of Pilocarpine on a Fasting Liver.

A.—*Last food* given about 26 hrs. before death, the food not eaten being removed 17 hrs. before death. (This is an exception to the rule generally followed.)

Subcutaneous injection of $\frac{1}{2}$ grain of pilocarpine (a little more than gram 0·03) was given 1 hr. 30 mins. before death.

B.—*Liver* apparently healthy.

Cells large and swollen looking.

Outline of the cells and the cellular mitoma extremely distinct.

Meshes of the mitoma very large.

Bile canaliculi large and distinct.

C.—These changes correspond to those observed in an active liver, and may be taken to indicate secretory activity.

Action of Pilocarpine on a Fed Liver.

A.—*Last food* given 7 hrs. before death.

Death blow 2 hrs. 43 mins. after a first subcutaneous injection of $\frac{2}{3}$ grain (gram 0·042) of pilocarpine (a second injection of the same quantity having been given 38 mins. before death).

B.—*Liver* moderately diseased, containing a few large psorospermic masses, and being somewhat above the average size.

Cells generally large but variable in size.

Outlines of cells and the *mitoma* even more distinct than normal.

Meshes of the mitoma large, specially round the nuclei.

Bile canaliculi indistinct.

Glycogen reaction about normal, slightly diminished.
Sugar reaction, 24 hrs. *post mort.*, slightly diminished.
Iron reaction much diminished, both in the diffuse and in the granular form.

C.—The changes produced in the fed liver correspond closely with those observed in the fasting organ, and may be taken as typical of secretory activity.

Action of Toluene on a Fasting Liver.

A.—*Last meal* 31 hrs. before death.
Rectal injection of 1 gram (15·5 grains) of toluene suspended in 10 c.c. of thin mucilage, 56 mins. before death.

B.—*Liver* of moderate size, with pretty abundant psorospermic lesions.
Cells small and medium sized.
Outline and mitoma clear, much clearer than normal.
A few large *meshes*, specially grouped round the nucleus.
Bile canaliculi not generally distinct, when distinct very narrow.
Glycogen reaction distinct round the hepatic vein, and therefore increased.
Sugar formed in 24 hrs. *post mort.*, much more abundant than normal.
Iron reaction almost absent, and therefore less than normal.

C.—The action resembles somewhat that of pilocarpine, but differs from it on account of the increase of glycogen.

Action of Toluene on the Fasting Liver.

A.—*Last meal* 20 hrs. before death.
Subcutaneous injection of about 0·06 gram (*i.e.*, = about 0·9 grain) of pure toluene 4 hrs. 45 mins. before death.

B.—*Liver* apparently not diseased.
Cells pretty large.
Outline of cells and mitoma more distinct than normal.
Meshes of mitoma a little larger than normal.
Bile canaliculi very distinct.
Blood capillaries rather congested.

C.—There is stimulation of the cells resembling, to a certain extent, that produced by pilocarpine, but much less marked.

Action of Toluene on a Fed Liver.

A.—*Last food* 8 hrs. before death.
Subcutaneous injection of about 0·06 gram of pure toluene 4 hrs. 53 mins. before death.

B.—*Liver* apparently not diseased.
Cells rather small.
Outline of cells and mitoma distinct.
Meshes large.
Bile canaliculi distinct here and there.
Blood capillaries excessively congested.

C.—With the exception of the size of the blood capillaries, there is no very marked departure from the normal.

Action of Benzol on a Starving Liver.

A.—*Last meal* 31 hrs. before death (a few very small bits of carrots were unfortunately left within reach of the animal during injection).
Rectal injection of 1·15 gram (*i.e.* 17·8 grains) of benzol, suspended in 10 c.c. of thin mucilage 2 hrs. 30 mins. before death.
Subcutaneous injection of about 0·5 c.c. of pure benzol 2 hrs. 5 mins. before death.

B.—*Liver* large, with abundant psorospermic lesions.
Cells pretty large.
Mitoma and outline distinct, much more so than normal.
Meshes of mitoma large.
Bile canaliculi very distinct, main canaliculi in portal zone.
Glycogen reaction very slightly increased, diffuse.
Sugar formed in 24 hrs. *post mort.*, very little, about normal.
Iron reaction very slight, normal ?

C.—The action is very similar to that of pilocarpine in every respect.
Note.—In this case it is possible that the munching of a few bits of carrot may have stimulated the liver; but the quantity so ingested was very small, and probably had no distinct effect.

Action of Benzol on a Fed Liver.

A.—*Last meal* 8 hrs. 34 mins. before death.
Rectal injection of 1 gram of benzol, suspended in 10 c.c. of thin mucilage, 1 hr. before death.

B.—*Liver* very large, the largest observed. Psorospermic lesions in moderate amount.

Cells very large, swollen-looking.

Mitoma and outline of cells very clear.

Meshes of mitoma large, specially round the nucleus.

Bile canaliculi indistinct.

Glycogen reaction very abundant round hepatic vein, somewhat diffuse elsewhere.

Sugar produced *post mort.* in 24 hrs. less than normal.

Iron reaction much diminished.

C.—This action resembles closely that of pilocarpine.

Action of Sodium Iodide on a Fasting Liver.

A.—*Last meal* 25 hrs. before death.

Rectal injection of 1·75 grams (*i.e.*, about 27 grains) of iodide of sodium dissolved in 10 c.c. of water 1 hr. before death.

B.—*Liver* medium sized, with very few psorospermic lesions.

Cells medium sized.

Mitoma and outline of cells pretty distinct.

Meshes of mitoma generally medium sized, some very large round the nuclei.

Bile canaliculi distinct at places but very small.

Glycogen, slight amount round the hepatic vein.

Sugar formed in 24 hrs. *post mort.*, the largest quantity produced except after toluylene diamine.

Iron reaction very indistinct, less than normal.

C.—Resembles pilocarpine except as regards the tendency of accumulation of glycogen.

Action of Sodium Iodide on a Fed Liver.

A.—*Last meal* 7 hrs. 40 mins. before death.

Rectal injection of 2 grams (31 grains) of sodium iodide dissolved in 10 c.c. of water 42 mins. before death.

B.—*Liver* larger than normal, psorospermic lesions very few.

Cells irregular, some very large, some small, angular.

Mitoma and outline of cells very distinct, more so than normal.

Meshes of the mitoma large, some very large round nuclei.

Bile canaliculi indistinct.

Glycogen, largest amount seen in any liver.

Sugar formed in 24 hrs. *post mort.*, large amount, perhaps a little more than normal.

Iron reaction very slight, less than normal.

C.—Action resembles that of pilocarpine, but in addition there is a marked tendency to accumulation of glycogen.

Action of Chrysophanic Acid on a Fasting Liver.

A.—*Last meal* 28 hrs. before death (animal allowed to eat a small bit of carrot during the injection).

Rectal injection of 0·1 gram (*i.e.*, about $1\frac{1}{2}$ grains) of chrysophanic acid suspended in 10 c.c. of thin mucilage 2 hrs. 23 mins. before death.

B.—*Liver* moderately large with very few psorospermic lesions.

Cells generally small or medium sized.

Outline of cells and *mitoma* clear, much more so than normal.

Meshes of mitoma generally small, a few large ones round the nucleus.

Bile canaliculi, main and lateral distinct.

Glycogen reaction increased, slight round the hepatic veins.

Sugar formed in 24 hrs. *post mort.*, more abundant than normal.

Iron reaction very slight, less than normal.

C.—This action resembles that of pilocarpine.

Action of Ammonium Chloride on a Fasting Liver.

A.—*Last meal* 28 hrs. before death.

Rectal injection of 1 gram (15·5 grains) of ammonium chloride dissolved in 10 c.c. of water 2 hrs. before death.

B.—*Liver* small, with very few psorospermic lesions.

Cells large.

Mitoma and outline of cells pretty distinct.

Meshes of mitoma large in some places.

Bile canaliculi generally indistinct.

Glycogen doubtful diffuse reaction (normal).

Sugar formed in 24 hrs. *post mort.*, very little (normal).

Iron reaction slight, about normal.

C.—Stimulation of the cells is indicated by the changes in the mitoma, similar to, but not so marked, as those produced by pilocarpine.

Action of Ammonium Chloride on a Fed Liver.

A.—*Last meal* 9 hrs. 20 mins. before death.

Rectal injection of 1 gram of chloride of ammonium in 10 c.c. of water (sp. gr. 1025) 1 hr. 5 mins. before death.

B.—*Liver* large, with few psorospermic lesions.
Cells large, looking swollen.
Mitoma and outline of cells very distinct (more than normal).
Meshes of mitoma large round the nucleus.
Bile canaliculi narrow, distinct only in portal zone.
Glycogen abundant, chiefly round the hepatic (more than normal).
Sugar formed in 24 hrs. *post mort.*, large amount (a little above normal).
Iron reaction entirely absent (much less than normal).

C.—This is a stimulating action similar to that of pilocarpine, but there seems to be in addition a tendency to the accumulation of glycogen.

Action of Toluylene Diamine (Meta) on a Fasting Liver.

A.—*Last meal* 29 hrs. before death. 4 hrs. 10 mins. before death, gram 0·5 (grains $7\frac{3}{4}$), suspended in 10 c.c. of mucilage, injected per rectum. 3 hrs. 36 mins. before death, gram 0·06 (*i.e.*, 1 grain), dissolved in 5 drops of benzol injected subcutaneously. 20 mins. before death, gram 0·06 given in a slice of carrot.

B.—*Liver* large, with pretty abundant psorospermic lesions.
Cells generally large, but variable in size.
Mitoma and outside of cells not very distinct, but clearer than normal.
Meshes of mitoma medium sized, larger than normal.
Bile canaliculi indistinct.
Glycogen reaction well marked round the hepatic vein, *i.e.*, more marked than normal.
Sugar formed in 24 hrs. *post mort.* more abundant than normal.
Iron reaction almost entirely absent.

C.—The action of toluylene diamine in this case resembles that of pilocarpine, except as regards the production of sugar *post mort.*

Action of Toluylene Diamine (Meta) on a Fasting Liver.

A.—Animal killed 24 hrs. after its *last meal.* A little under gram 0·5 (= 7 grains), finely divided, and suspended in 10 c.c. of water, injected per rectum 2 hrs. 13 mins. before death.

B.—*Liver* moderately large, a pretty large number of psorospermic lesions were present.
Cells generally large.

Mitoma and outline of cells more distinct than normal.
Meshes large.
Bile canaliculi where distinct small, but generally indistinct.
Glycogen reaction increased immediately round the hepatic vein.
Post-mortem production of sugar in 24 hours more marked than in any other case.
Iron reaction almost absent.

C.—With the exception of the *post mort.* production of sugar this action resembles closely that of pilocarpine.

Action of Toluylene Diamine (Meta) on a Liver immediately after the taking of Food.

A.—*Last ordinary meal* 25 hrs. before death; 17 *hrs.* 30 *mins. before death* the animal was given carrots with gram 0·09 of toluylene diamine; 1 hr. 30 mins. before death a new dose of 0·06 gram of toluylene diamine was given with 10 grams of carrots by the mouth.

B.—*Liver* pretty large, psorospermic lesions pretty abundant.
Cells large.
Mitoma and outline very distinct.
Meshes large, chiefly round the nucleus.
Bile canaliculi generally indistinct; where distinct, small.
Glycogen reaction slight round the hepatic vein (about normal).
Sugar formed in 24 hrs. *post mort.*, more abundant than normal.
Iron reaction entirely absent, normal.

C.—Action similar to that of pilocarpine, with the exception of the production of sugar *post mort.*

Action of Nitric Acid on a Starving Liver.

A.—*Last meal* 25 hrs. before death.
Rectal injection of 1 c.c. of nitric acid diluted in 10 c.c. of water (sp. gr. 1024), 1 hr. 15 mins. before death.

B.—*Liver* large, with few psorospermic lesions.
Cells small or medium-sized.
Mitoma and outline of cells not very distinct, but more so than normal.
Meshes of mitoma distinctly larger than normal.
Bile canaliculi, main very distinct, lateral often distinct.
Glycogen reaction doubtful, diffuse, normal.
Sugar formed *post mort.* in 24 hrs., very small amount, about normal.
Iron reaction very slight, less than normal.

C.—The action resembles much that of pilocarpine.

Action of Nitric Acid on a Fed Liver.

A.—*Last food* 7 hrs. 45 mins. before death.

Rectal injection of 0·5 c.c. of nitric acid diluted with 10 c.c. of water (sp. gr. 1011 to 1012) 50 mins. before death.

B.—*Liver* medium size, quite healthy.

Cells large, swollen looking.

Mitoma and outline of cells very clear, normal.

Meshes of mitoma large round the nucleus (normal).

Bile canaliculi indistinct.

Glycogen very slightly increased.

Sugar formed in 24 hrs. *post mort.*, normal amount.

Iron reaction much less than normal.

C.—This action resembles closely that of pilocarpine.

Action of Aniline on a Starved Liver.

A. This experiment is not quite comparable with the others. A rabbit, after being treated in the usual way, received *an injection* of 1 gram of *acetate of ammonium* per rectum, and 20 mins. afterwards another 1·5 gram. This apparently produced no effect, and the rabbit was not killed. It *was then fed* 42 hrs. before its death; $\frac{3}{4}$ hr. before it was killed, 1 gram of aniline thoroughly mixed with water was injected into the rectum. This produced well-marked symptoms, as in XXIII.

B.—There were few psorospermic lesions, the *liver* was very small.

Cells unequal; some small, some medium size.

Mitoma and outlines of cells indistinct generally, but distinct at places.

Meshes generally small.

Main bile canaliculi distinct in the portal zone.

Glycogen reaction indistinct, diffuse.

Sugar produced in 24 hrs. *post mort.*, very small.

Iron reaction considerably increased.

C.—The secretory activity of the liver did not seem to be much affected by aniline, but this substance seems to have had destructive action on some cells, and has caused a considerable splitting of organic compounds containing iron. In certain parts the cells were dropsical and possibly necrosed.

Action of Aniline on a Fasting Liver.

A.—*Last meal* 25 hrs. before death.

1 gram (15·5 grains) of pure aniline mixed with 10 c.c. of water *injected* into the rectum 1 hr. 32 mins. before death.

B.—*Liver* of small size with only a few psorospermic lesions.
Liver cells medium sized.
Outline of cells and mitoma indistinct (*i.e.*, normal in appearance).
Meshes of the mitoma small, normal in appearance.
Bile canaliculi, main and lateral, very distinct.
Glycogen reaction doubtful, diffuse, normal.
Sugar produced in 24 *hrs. post mort.* a little more than normal.
Iron reaction slight and round hepatic veins, *i.e.*, normal.

C.—Aniline in this case does not seem to have produced any marked effect on the liver.

Action of Phenol on a Fasting Liver.

A.—*Last food* given 25 hrs. before death.
Rectal injection of 0·83 gram (about 12 grains) of absolute phenol dissolved in 10 c.c. of water 46 mins. before death.

B.—Moderate amount of psorospermic lesions.
Liver moderately large.
Cells small, but not below normal.
Mitoma and outline of cells indistinct, but not more so than normal.
Meshes of mitoma generally small, irregular.
Glycogen reaction indistinct, about normal.
Sugar produced in 24 hrs. *post mort.* very slightly increased.
Iron reactions not very distinct, altered.

C.—Phenol does not seem in this case to produce marked alterations of secretory activity.
Note.—The cells are in many places much vacuolated, breaking down, and probably in a state of incipient necrosis.

Action of Phenol on a Fed Rabbit.

A.—*Time of last meal*, 7 hrs. 15 mins. before death.
0·5 gram (about $7\frac{3}{4}$ grains) of phenol dissolved in 10 c.c. of water *injected* into the rectum 50 mins. before death.

B.– Psorospermic lesions of the liver moderately abundant.
Organ large.
Cells large.
Outline of cells and mitoma clear, but less so than normal.
Size of the meshes of the mitoma a little less than normal.
Bile canaliculi generally indistinct.
Glycogen reaction much diminished and diffuse.

Sugar obtained in 24 hrs. *post mort.*, a little more than half the normal amount.

Iron reaction considerably increased.

C.—Phenol in this case evidently interfered with constructive metabolism, and caused an increased decomposition of organic compounds containing iron.

Note.—In this case there were also evidences of beginning necrosis of patches of liver cells.

Action of Atropine on a Fed Liver.

A.—*Last food* given 5 hrs. 45 mins. before death.

6 hrs. 30 mins. before death a *subcutaneous injection* of $\frac{1}{60}$ of a grain was given, $\frac{1}{4}$ hr. after another $\frac{1}{60}$ grain, and after another $\frac{1}{4}$ hour $\frac{1}{50}$ grain. Afterwards successive doses of $\frac{1}{10}$ grain of atropine were given with the food up to nearly $\frac{1}{2}$ grain (0·03 gram); the animal being thus saturated with atropine both before and during the last meal.

B.—*Liver* considerably altered by psorospermic lesions, but about normal in size.

Cells large.

Outlines of cells and the mitoma very indistinct.

Meshes of the mitoma generally small, but a few large ones were faintly indicated.

Bile canaliculi generally indistinct; where distinct they were very narrow.

Glycogen reaction well marked, but less so at the periphery of the lobule than it should have been.

Iron reaction did not show anything special.

C.—These changes are taken as the type of a liver in which the secretory activity is diminished.

I. *Action of Atropine on a Fed Liver.*

A.—*Last food* given 7 hrs. before death.

Subcutaneous injection of $\frac{1}{75}$ of a grain (gram 0·002) of sulphate of atropine was given 3 hrs. 30 mins. before death.

B.—There were only a few psorospermic lesions in the organ.

Cells large.

Outlines of the cells and the mitoma not very distinct.

Meshes of the mitoma small.

Bile canaliculi, where distinct, were narrow.

C.—These appearances were those of a fasting liver, with the ex-

ception of the size of the cells, and are taken to correspond to diminished secretory activity.

Action of Ammonia on a Fasting Liver.

A.—*Last food* given 25 hrs. before death.

1 c.c. of liquor ammoniæ, diluted with 9 c.c. of water, was *injected* into the rectum 12 mins. before death (death accidental, possibly accelerated by, but not, certainly, due to the drug).

B.—*Liver* very slightly diseased (psorospermosis) and of small size.

Cells small.

Mitoma more indistinct than normal, and the cellular cleavage also.

Meshes of the mitoma smaller than normal.

Bile canaliculi seldom distinct.

Glycogen reaction normal, *i.e.*, there were no distinct glycogenic granules.

Sugar reaction, obtained after maceration in water for 24 hrs., was a little more marked than under normal circumstances.

Iron reaction considerably increased, but diffuse.

C.—Ammonia seemed in this case to have an action somewhat similar to that of atropine, but to cause a greater splitting of organic combinations of iron.

Action of Ammonia on a Fed Liver.

Last food given 8 hrs. and 30 mins. before death.

1 c.c. of liquor ammoniæ, diluted with 10 c.c. of water, was administered per rectum 65 mins. before death.

B.—*Liver cells* rather large.

Outline of the cells and the cytomitoma indistinct, instead of being very distinct, as they should have been.

Meshes of the mitoma small instead of large.

Bile canaliculi generally indistinct.

Glycogen reaction well marked in the hepatic zone only, instead of being more general.

Sugar produced in 24 hrs. after death was normal.

Iron reaction more marked than normal, but was diffuse; the granules were, on the contrary, rather less than normal.

C.—Generally speaking, the results were the same as in the fasting state, and, with the exception of the changes in the iron reaction, were similar to those produced by atropine.

Provisional Conclusions.

The effect which the administration of various drugs has on the distinctness of the cellular mitoma and on the distribution or arrangement of that mitoma and of the paramitoma, resembles, in the case of a certain number of drugs, that of pilocarpine, and in others that of atropine. The first drugs may be said to stimulate glandular activity, the latter to restrain it; only a few of those experimented with seemed to have neither a stimulating nor a depressing action.

On this basis we may subdivide the compounds studied into three groups.

1. Stimulating or *excito-secretory group*, with pilocarpine for a type.
2. Neutral group.
3. Depressing or *depresso-secretory group*, with atropine for type.

1. *Excito-secretory group.*

Of the following compounds, those heading the following list produced the most marked changes in the mitoma of the cells:—

Toluene, benzol, sodium iodide, pilocarpine, chrysophanic acid, ammonium chloride, toluylene diamine, nitric acid.

(Aniline seemed in one case to have a stimulating effect, but this was doubtful.)

2. *Neutral group.*

No drug was altogether neutral, but two drugs seemed to have little depressing, and still less exciting, action, though they evidently produced degenerative changes in the cells; in the doses used, they acted probably too powerfully as poisons. These compounds were aniline and phenol.

3. *Depresso-secretory group.*

The following compounds belong to this group:—

Phenol, atropine, ammonia.

In each of the two great groups it is possible to recognise marked differences based on the influence which the drugs had (1) on the storage of glycogen; (2) on the accumulation of compounds giving the reaction of inorganic ferric salts in the liver.

1. In the *excito-secretory* group.

* *Glycogenic Function.*

A.—The following drugs *caused marked increase of glycogen in the liver*:—

Sodium iodide, toluylene, diamine, chrysophanic acid (toluene?) (ammonium chloride?)

B.—The following gave rise to *no marked increase of glycogen*, and sometimes even to a diminution:—

(Ammonium chloride?), nitric acid, pilocarpine, benzol.

*** Ferrogenic Function.*

A.—The following drugs caused *a very marked diminution in the amount of free iron in the liver*:—

Sodium iodide, toluene, toluylene diaminc.

B.—The following caused *a diminution in the quantity of iron, but not to the same extent* as the first, and the iron was oftcn so distributed as to remind one of the appearances observed in an active liver:—

Chloride of ammonium, nitric acid, pilocarpine, benzol (in the fed liver).

C.—*In one case only a doubtful increase of iron was found*:—

Benzol (in the fasting liver).

2. In the group of *depresso-secretory compounds.*

A.—*Ammonia* caused a diminution of the glycogen and an increase of iron.

By its influences on the accumulation of glycogen and of iron, *phenol* acts distinctly in the same way as the depresso-secretory compounds; thus it caused diminution in the glycogen and an increase in the iron.

Aniline caused little change in the glycogen, but a great accumulation of iron in one case. The action of aniline evidently requires to be studied more specially.

B.—*Atropine* caused a slight diminution in the glycogen and little change in the iron.

General Concluding Remarks.

We are satisfied that much is to be learned of the *affinities of drugs* and of their *physiological action* by the methods which we have been using in this study. The anticipation of unknown difficulties in a field practically new has caused us to spend much time in observations which have not all proved of much use. We know now how to obtain those results which are most useful. We are repeating some of the cxperiments in order to test the value of our first results, and we are slowly repeating the measurements which have already taken such a considerable amount of time. It would be unwise in the present state of the inquiry to attempt to give more dogmatic conclusions than those we offer provisionally.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.